WHAT IS CLAIMED IS:

1. A nucleic acid molecule comprising:

an RNA polymerase III promoter sequence;

a short RNA encoding sequence comprising a transcription initiation site;

a *loxP*-flanked STOP cassette comprising an RNA polymerase III-specific termination sequence, a first *loxP* sequence, and a second *loxP* sequence, wherein (i) each of the two *loxP* sequences comprises a spacer region, (ii) the termination sequence is disposed between the first and second *loxP* sequences, and (iii) the termination sequence is disposed between the promoter sequence and the transcription initiation site of the short RNA encoding sequence in the nucleic acid molecule.

2. The molecule of claim 1, wherein each of the *loxP* sequences comprises one or more mutations in its spacer region.

3. The molecule of claim 1, wherein the first *loxP* sequence is a wild-type *loxP* sequence.

4 The molecule of claim 1 or 3, wherein the second *loxP* sequence is a mutant *loxP* sequence.

5. The molecule of any one of claims 1 to 4, wherein

the second *loxP* sequence is closer to the short RNA encoding sequence that the first *loxP* sequence;

the second *loxP* sequence comprises a distal terminal sequence and a proximal terminal sequences, wherein the spacer region is disposed between the distal and the proximal terminal sequence, the distal terminal sequence is closer to the termination sequence than the spacer region, and the proximal terminal sequence is closer to the shRNA encoding sequence than spacer region;

the second *loxP* proximal terminal sequence overlaps with 1 to 10 nucleotides of 5' end of the short RNA encoding sequence; and

the 1 to 10 nucleotides of the 3'end of the second *loxP* proximal terminal sequence consists of the 5'end of the short RNA encoding sequence.

6. The molecule of any one of claims 1 to 5, further comprising a thymidine nucleotide immediately preceding the upstream terminal sequence of the first *loxP*, wherein the first *loxP* is upstream of the termination sequence.

7. The molecule of any one of claims 1 to 6, wherein the RNA polymerase III promoter sequence comprises genomic sequence of the small nuclear RNA U6 promoter or a functional equivalent thereof.

8. The molecule of claim 7, wherein:

the termination sequence comprises genomic sequence downstream of the small nuclear RNA U6 transcription termination signal.

9. The molecule of claim 8, wherein the termination sequence is a modified U6 transcription termination sequence comprising:

between 1 to 20, inclusive, additional thymidine nucleotides disposed immediately adjacent to the wild-type U6 thymidine termination signal; and

between 1 to 190, inclusive, additional nucleotides of animal genomic sequence that is immediately downstream of the thymidine termination sequence of wild-type small nuclear RNA U6 gene.

10. The molecule of claim 8 or 9, wherein the termination sequence further comprises one or more additional RNA Polymerase III termination signals.

11. The molecule of any one of claims 1 to 10, wherein the short RNA encoding sequence encodes a transcript with fewer than 30 nucleotides.

12. The molecule of any one of claims 1 and 3 to 11, wherein the molecule comprises a sequence selected from the group consisting of: SEQ ID NOs: 1 to 7.

13. A transgenic animal whose genome comprises the nucleic acid molecule of any one of claims 1 to 12.

14. The transgenic animal of claim 13, further comprising a nucleic acid molecule encoding a Cre recombinase.

15. The transgenic animal of claim 14, wherein expression of the Cre recombinase is developmentally regulated.

16. The transgenic animal of claim 13, wherein expression of the Cre recombinase is tissue-specific.

17. The animal of any one of claims 12 to 16, wherein the animal is selected from the group consisting of a mouse, a rat, a guinea pig, a goat, a pig, a monkey, a baboon, a chimpanzee, a cow, a rabbit, a sheep, a dog, a cat, a hamster, a chicken, and a frog.

18. A eukaryotic cell comprising the nucleic acid molecule of any one of claims 1 to 12.

19. The cell of claim 18, wherein the cell is an animal cell.

20. The cell of claim 18, wherein the cell is a mammalian cell.

21. The cell of claim 19 or 20, wherein the cell is an embryonic stem cell.

22. The cell of any one of claims 18 to 21, further comprising a nucleic acid molecule encoding a Cre recombinase gene.

23. The cell of any one of claims 18 to 21, further comprising a Cre recombinase protein.

24. A method of making an inducible short RNA expression system, the method comprising linking two or more nucleic acids to produce the nucleic acid of any one of claims 1 to10.

25. A method of making a transgenic animal comprising:

introducing the molecule of any one of claims 1 to 12 into the genome of an embryonic stem cell;

introducing the embryonic stem cell into an embryo;

implanting the embryo in an animal capable of carrying the embryo to term; and

allowing the embryo to come to term, thereby generating a transgenic animal.

26. The method of claim 25, wherein:

the molecule of any one of claims 1 to 12 is introduced into the genome of an oocyte;

the oocyte is fertilized to produce an embryo;

the embryo is implanted in an animal capable of carrying the embyo to viability; and

the embryo is allowed to become a viable animal, thereby generating a founder transgenic animal.

27. The method of claim 25, wherein the method generates a chimeric transgenic animal, and further comprising:

crossing the chimeric transgenic animal to another animal of the same species to generate a founder transgenic animal whose genome includes the molecule of any one of claims 1 to 12.

28. A method of making an animal cell containing an inducible short RNA expression, the method comprising:

transfecting a cell with the molecule of any one of claims 1 to 12.

29. The method of claim 28, wherein the cell is a cell from any one of the following animals: a human, a mouse, a rat, a guinea pig, a goat, a pig, a monkey, a baboon, a chimpanzee, a cow; a horse, a rabbit; a sheep, a chicken, a dog, a cat, a frog, or a fish.

30. A method of evaluating gene function in a cell, the method comprising:

providing the cell of any one of claims 18 to 23;

inducing transcription of the short RNA encoding sequence; and

monitoring changes in the cell.

31. A method of evaluating gene function in an organism, the method comprising:

providing the transgenic animal of any one of claims 13 to 17;

inducing transcription of the short RNA encoding sequence; and

monitoring changes in the organism.

32. A method of treating a patient, the method comprising:

administering the molecule of anyone of claim 1 to 12 into a patient in need of having expression of one or more genes reduced, wherein the short RNA encoding sequence encodes a transcript designed to reduce expression of the one or more genes the patient is in need of reducing.

33. The method of claim 32, wherein the method comprises administering the molecule in the cell of any one of claims 18 to 23.

34. A method of identifying a candidate RNAi effector with reduced activity in T-cells, the method comprising:

administering or inducing expression of siRNA in a T-cell and a control cell;

evaluating expression of an mRNAs or protein in the T-cell and the control cell; and

identifying an mRNA or protein (a) with a reduced expression level or (b) that is differently modified in the T-cell relative to control,

wherein the control cell is not a mature lymphocyte and an mRNA or protein with reduced levels or that is differently modified in the T-cell relative to control is a candidate RNAi effector with reduced activity in T-cells.

35. A method of identifying a candidate inhibitor of RNAi in T-cells, the method comprising:

administering or inducing expression of siRNA in a T-cell and a control cell;

evaluating expression of an mRNA or protein in the T-cell and the control cell; and

identifying an mRNA or protein (a) with an increased expression level or (b) that is differently modified in the T-cell relative to control;

wherein the control cell is not a mature lymphocyte and an mRNA or protein with reduced levels or that is differently modified in the T-cell relative to control is a candidate inhibitor of RNAi in T-cells.

36. A method of identifying a missing RNAi effector or inhibitor of RNAi in T-cells, the method comprising:

identifying a candidate missing RNAi effector or candidate inhibitor of RNAi by performing the method of claim 34 or 35; and

(i) in one or more T-cells, (a) introducing the identified candidate RNAi effector or (b) modifying the identified candidate RNAi effector, and subsequently determining if (a) or (b) increases RNAi efficiency in the one or more T-cells, wherein an increases RNAi efficiency is an RNAi effector with reduced activity in T-cells;

(ii) introducing or modifying the identified candidate inhibitor of RNAi in a cell, and subsequently determining if it reduces RNAi efficiency in the cell, wherein a candidate that reduces RNAi efficiency in the cell is an inhibitor of RNAi in T-cells; or

(iii) inactivating the identified candidate inhibitor in a T-cell, and subsequently determining if inactivation increases RNAi efficiency in the T-cell, wherein an inactivated candidate inhibitor that increases RNAi efficiency in the T-cell is an inhibitor of RNAi in T-cells.